# **Electronic Supplementary Information**

# Expanding the biological utility of bis-NHC gold(I) complexes through post synthetic carbamate conjugation

Sajal Sen, Yue Li, Vincent Lynch, Kuppuswamy Arumugam, Jonathan L. Sessler and Jonathan F. Arambula

University of Texas at Austin Wright State University

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# Materials and general methods:

### **General considerations:**

All chemical reactions were conducted under nitrogen atmosphere using Schlenk techniques. The glassware was oven dried at 120 °C before use. All materials were obtained from commercial sources at the highest purity available and used without further purification. Chloro (dimethylsufide) gold(I) was purchased from Sigma-Aldrich. [Au(IPr)OH] (2) was synthesized according to the procedure of Nolan et al.<sup>1</sup> Complex **3** was also synthesized according to previously published protocols.<sup>2</sup> Solvents were either dried with a solvent purification system (DCM, acetonitrile, methanol) or dried over molecular sieves (toluene) (3 Å) and degassed prior to use.

The reported <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were measured on Varian Inova spectrometers at The University of Texas at Austin using  $CD_2Cl_2$  and DMSO- $d_6$  as deuterated solvents. The chemical shifts were reported relative to the residual solvent proton signals. For the spin multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet) and m (multiplet), as well as appropriate combinations of these. Coupling constants for protons (*J*) are given in Hertz (Hz). The NMR spectra were analyzed using the software *MestReNova v.10.0.2-15465* (Mestrelab Research S.L.) All deuterated solvents were purchased from Cambridge Isotope Laboratories. High-resolution electrospray ionization (ESI) mass spectra were recorded on a VG ZAB2E instrument or VG AutoSpec apparatus. Column chromatography was performed on Sorbent silica gel (40-63 µm). Analytical thin layer chromatography (TLC) analyses were carried on glass-backed silica gel plates (200 µm, Sorbent Technologies). Fluorescence measurements were performed at room temperature on a Photon Technology International fluorimeter.

Common abbreviations used:

**DCM** = Dichloromethane. **DEE** = Diethyl ether. **TEA** = Triethylamine. **ACN** = Acetonitrile.

# Synthesis:

Synthesis of [1][Br]:



Compound 2 (250 mg, 0.414 mmol, 1 equiv.) and 3 (142 mg, 0.456 mmol, 1.1 equiv.) were combined in an oven-dried 20 ml scintillation vial containing 4 ml of dry toluene. The mixture was stirred for 18 h at 90 °C, which led to the appearance of a white precipitate. The precipitate was filtered using a Buchner funnel and washed with toluene and then pentane two times. After collecting the precipitate, 4 ml nanopure water was added and the resulting mixture was left stirring for 15 min to remove any residual imidazolium bromide salt. Thereafter, the white precipitate was filtered again and the resulting solid was washed with 3 ml water and diethyl ether twice. The resulting solid was then collected and dried under vacuum to afford [1][Br] as a white microcrystalline powder.

Yield: 260 mg (70%).

**ESI-HRMS (acetonitrile) (m/z)**: calculated for  $[C_{41}H_{54}AuN_4O]^+$ : 815.3958, obtained: 815.3960.

<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  8.05 (s, 2 H), 7.60 (t, 2 H, *J*= 7.77 Hz), 7.48 (s, 1 H), 7.33 (d, *J*= 7.80, 4 H), 7.26 (s, 1 H), 6.77 (s, 1 H), 4.89 (br s, 1 H), 3.64 (t, *J*= 5 Hz, 2 H), 3.20 (dd, *J* = 4.90 Hz, 4.91 Hz, 2 H), 2.35 (m, 7 H), 1.56 (s, 6H), 1.17 (d, *J*= 6.80 Hz, 12 H), 1.07 (d, *J*= 6.86 Hz, 12 H). Small toluene peaks can be seen even after 12 h vacuum drying.  $\delta$  7.25 (m),  $\delta$  7.18 (m),  $\delta$  2.30 (s).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.34, 181.86, 145.35, 138.72, 134.56, 134.11, 133.94, 125.41, 124.23, 123.13, 61.30, 52.92, 28.84, 24.23, 21.34, 17.16. Small toluene peaks can be seen even after 12 h vacuum drying. δ 137.84, 129.36, 128.68, 125.79, 21.46.

Synthesis of [1][PF<sub>6</sub>]:



[1][Br] (250 mg, 0.279 mmol, 1 equiv.) was dissolved in 1 ml methanol and NaPF<sub>6</sub> (281 mg, 1.674 mmol, 6 equiv.) in 4 ml nanopure water was added. The mixture was stirred overnight and the precipitate was filtered. The white solid was washed with 5 ml water and finally with 5 ml hexanes twice. The solid was dried under vacuum and collected as white fluffy powder.

Yield: 258 mg (97%).

**ESI-HRMS (acetonitrile) (m/z):** Positive mode: calculated for  $[C_{41}H_{54}AuN_4O]^+$  815.3958, obtained: 815.3964. Negative mode: (ESI-MS): 145.0 [PF<sub>6</sub>]<sup>-</sup>.

<sup>1</sup>**H** NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  8.05 (s, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 4H), 7.26 (d, *J* = 1.8 Hz, 1H), 6.77 (s, 2H), 4.89 (t, *J* = 4.9 Hz, 2H), 3.64 (t, *J* = 5.0 Hz, 2H), 3.20 (q, *J* = 4.9 Hz, 2H), 2.35 (q, *J* = 7.0 Hz, 7H), 1.56 (s, 6H), 1.17 (d, *J* = 6.8 Hz, 12H), 1.07 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>**C NMR (DMSO-***d***<sub>6</sub>):** δ (ppm) 186.34, 181.86, 145.35, 138.72, 134.56, 134.11, 133.94, 125.41, 124.23, 123.13, 61.30, 52.92, 28.84, 24.23, 21.34, 17.16.

**Elemental Analysis:** Calculated for  $[C_{41}H_{54}AuN_4O][PF_6]$ : C, 51.25; H, 5.67; N, 5.83. Found: C, 51.37; H, 5.70; N, 5.88.

#### Synthesis of 4:



[1][PF<sub>6</sub>] (200 mg, 0.208 mmol, 1 equiv.) and 4-nitrophenylchloroformate (335 mg, 1.664 mmol, 8 equiv.) were combined in an oven-dried two-neck round bottom and kept under vacuum for 15 min. 7 ml of dry DCM and dry triethylamine (44  $\mu$ l, 0.312 mmol, 1.5 equiv.) were added to the mixture. The clear solution was stirred for 48 h to achieve the full conversion as indicated by LCMS. The DCM was evaporated off and diethyl ether was added. A white solid precipitated out after stirring for 15 mins and trituration. The solid obtained in this way was collected via filtration and washed several times with diethyl ether. (Note: If water is added to the filtrate, it turns yellow indicating the presence of 4-nitrophenol.) The solid was placed in a 20 ml scintillation vial and 5 ml of nanopore water was added. The reaction mixture was then stirred for 15 min. Finally, the resulting white suspension was filtered, washed with 5 ml water and diethyl ether and left to dry under air.

**Yield:** 185 mg (79%).

ESI-HRMS (acetonitrile) (m/z): Calculated for  $[C_{48}H_{57}AuN_5O_5]^+$  980.4020 obtained: 980.4025.

<sup>1</sup>**H** NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  8.36 – 8.30 (m, 2H), 8.07 (s, 2H), 7.73 (d, *J* = 2.0 Hz, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.46 – 7.40 (m, 2H), 7.37 (d, *J* = 1.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 4H), 6.76 (s, 2H), 4.12 (t, *J* = 5.0 Hz, 2H), 3.96 (t, *J* = 5.1 Hz, 2H), 2.42 – 2.30 (m, 7H), 1.54 (s, 6H), 1.17 (d, *J* = 6.9 Hz, 12H), 1.09 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>**C NMR (DMSO-***d***<sub>6</sub>):** δ (ppm) 186.39, 181.85, 145.43, 138.77, 134.56, 133.94, 130.89, 129.46, 125.41, 124.29, 123.13, 61.30, 52.92, 28.71, 24.25, 24.08, 21.25, 17.21.

**Elemental Analysis:** Calculated for C<sub>48</sub>H<sub>57</sub>AuN<sub>5</sub>O<sub>5</sub>PF<sub>6</sub>: C, 51.20; H, 5.10; N, 6.22. Found: C, 51.14; H, 5.13; N, 6.19.

### General synthesis of carbamates via Protocol 1:

Precursor 4 (1 equiv.) was kept under vacuum for 15 mins in an oven-dried two-neck round bottomed flask. Dry DCM (4 ml) and the amine of interest (2-3 equiv.) were then added. After stirring the mixture for 10 min, dry TEA (2 equiv.) was added and whole mixture was stirred under  $N_2$  atmosphere for 12-36 h. After confirming the completion of the reaction by LCMS, the DCM was evaporated and to that diethyl ether was added. The solid precipitate was subsequently filtered. Finally, the solid was collected and 4 ml of nanopore water was added to it and stirred for another 15 min. The remaining solid was filtered and washed with 5 ml water and hexanes respectively.

#### Synthesis of 5:



### Reaction Time: 12 h

4 (50 mg, 0.044 mmol, 1 equiv.) was used along with  $NH_2NH_2.xH_2O(N_2H_4:60\%)$  (8 µl, ~3 equiv.) and dry TEA (10 µl, 0.071 mmol, 1.6 equiv.). White microcrystalline powder. Crystals were grown using DCM/DEE and via slow diffusion.

**Yield:** 35 mg (79%)

**ESI-HRMS (acetonitrile) (m/z):** Calculated for  $[C_{42}H_{56}AuN_6O_2]^+$  873.4125 obtained : 873.4123.

<sup>1</sup>**H** NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  8.13 (s, 1H), 8.07 (s, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.48 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 5H), 6.77 (s, 2H), 4.02 (s, 2H), 3.80 (t, *J* = 5.2 Hz, 2H), 3.71 (d, *J* = 5.4 Hz, 2H), 2.35 (d, *J* = 7.3 Hz, 7H), 1.56 (s, 6H), 1.17 (d, *J* = 6.8 Hz, 12H), 1.08 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 185.88, 182.28, 157.51, 145.45, 138.87, 134.39, 134.10, 133.89, 130.95, 129.48, 126.88, 125.46, 123.67, 124.28, 63.25, 49.78, 28.72, 24.30, 24.07, 21.26, 17.21.

#### Synthesis of 6:



#### Reaction time: 24 h

4 (40 mg, 0.035 mmol, 1 equiv.) was used along with N-Boc-ethylenediamine (17  $\mu$ l, 0.105 mmol, 3 equiv.) and dry TEA (10  $\mu$ l, 0.071 mmol, 2 equiv.). White microcrystalline powder. Crystals were grown using DCM/DEE, via slow diffusion, but they were too thin to mount.

**Yield:** 21 mg (53%)

**ESI-HRMS (acetonitrile) (m/z):** Calculated for  $[C_{49}H_{68}AuN_6O_4]^+$ : 1001.4962 observed: 1001.4961.

<sup>1</sup>**H NMR (500 MHz, DMSO-***d*<sub>6</sub>**):**  $\delta$  8.07 (s, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 1.9 Hz, 1H), 7.36 – 7.30 (m, 5H), 7.05 (d, *J* = 5.7 Hz, 1H), 6.79 (d, *J* = 5.7 Hz, 1H), 6.76 (s, 2H), 3.78 (t, *J* = 5.4 Hz, 2H), 3.71 (t, *J* = 5.2 Hz, 2H), 2.98 – 2.93 (m, 3H), 2.35 (q, *J* = 6.6 Hz, 7H), 1.56 (s, 6H), 1.37 (s, 9H), 1.17 (d, *J* = 6.8 Hz, 12H), 1.08 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>**C NMR (DMSO-***d*<sub>6</sub>): δ 186.19, 182.30, 156.09, 155.68, 145.45, 138.86, 134.40, 134.10, 133.90, 130.94, 129.48, 125.46, 124.27, 124.06, 123.62, 78.17, 62.95, 49.92, 28.72, 28.68, 24.29, 24.07, 21.25, 17.19.

**Elemental Analysis:** Calculated for  $C_{49}H_{70}AuN_6O_5PF_6$ : C, 50.52; H, 6.06; N, 7.21. Found: C, 50.83; H, 6.10; N, 7.12.

### Synthesis of 7:



#### **Reaction time:** ~ 47 h

DOX•HCl (40 mg, 0.0735 mmol, 2.1 equiv.) was dissolved in 0.2 ml dry DMF, 12 ml dry DCM and 0.080 ml dry TEA (0.582 mmol, 16 equiv.) and stirred for 30 mins. Next, 4 (40 mg, 0.035 mmol, 1 equiv.) dissolved in 1 ml dry DCM was added. The reaction progress was monitored over time. It was noticed that after ~47 h, the reaction is complete as determined by TLC analysis. The DCM was evaporated off and DEE was added; this produced a dark red solid. This red solid (15 mg) was dissolved in 2 ml ACN:water (55:45 v/v). The resultant mixture was purified via HPLC using ACN:water 75:25 as the eluent to provide a retention time ~24.5 min. The pure fractions were collected and combined together. Finally, they were lyophilized to get pure dry product.

Yield: 8 mg (15%)

**ESI-HRMS (acetonitrile) (m/z): Positive mode-** Calculated for  $[C_{69}H_{81}AuN_5O_{13}]^+$ : 1384.5497, obtained : 1384.5505. Negative mode-  $[PF_6]^-$ : 145.1.

<sup>1</sup>**H** NMR (500 MHz, dichloromethane- $d_2$ ):  $\delta$  13.94 (s, 1H), 13.21 (s, 1H), 7.94 (d, J = 7.7 Hz, 1H), 7.73 (t, J = 8.1 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.33 (d, J = 8.5 Hz, 1H), 7.20 – 7.11 (m, 5H), 7.05 (d, J = 1.9 Hz, 1H), 6.61 (d, J = 1.8 Hz, 1H), 6.47 (s, 1H), 6.39 (s, 1H), 5.39 (d, J = 3.7 Hz, 1H), 5.19 (t, J = 3.0 Hz, 1H), 5.13 (d, J = 8.8 Hz, 1H), 4.67 (s, 2H), 4.48 (s, 1H), 4.00 (q, J = 6.6 Hz, 1H), 3.93 (s, 3H), 3.68 – 3.52 (m, 4H), 3.49 (d, J = 2.6 Hz, 1H), 3.20 (dd, J = 18.6, 2.0 Hz, 1H), 2.97 (d, J = 18.7 Hz, 1H), 2.29 (pd, J = 7.1, 4.3 Hz, 4H), 2.19 (s, 3H), 1.41 (d, J = 4.1 Hz, 6H), 1.21 – 1.16 (m, 3H), 1.08 (d, J = 6.8 Hz, 12H), 1.00 (dd, J = 16.4, 6.9 Hz, 12H).

HPLC trace of the reaction for conjugate 7:



#### **Retention time (mins)**

**Fig. S1.** Reaction progress for **7** as monitored by HPLC at various time points: t = 0 h, 3 h, 8 h, 23 h, 30 h, 35 h, and 47 h.

HPLC trace of isolated product:



Retention time (min)

Fig. S2. HPLC trace of isolated product monitored at 470 nm.



Retention time (min)

Fig. S3. HPLC trace of isolated product monitored at 254 nm



LCMS of 7



HRMS analysis of 7

#### Synthesis of 8:



#### Reaction time: 24 h

Precursor 4 (40 mg, 0.035 mmol, 1 equiv.) was combined with morpholine (9  $\mu$ l, 0.105 mmol, 3 equiv.) and dry TEA (10  $\mu$ l, 0.071 mmol, 2 equiv.) per the general procedure above. This gave 8 as a white microcrystalline powder. Crystals were grown from DCM/DEE via slow diffusion.

**Yield:** 23 mg (61%)

**ESI-HRMS (Acetonitrile) (m/z):** Calculated for  $[C_{46}H_{61}AuN_5O_3]^+$ : 928.4434 observed: 928.4451.

<sup>1</sup>**H NMR (500 MHz, DMSO-***d*<sub>6</sub>**):**  $\delta$  8.07 (s, 2H), 7.64 (d, *J* = 1.9 Hz, 1H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 5H), 6.77 (s, 2H), 3.91 – 3.79 (m, 4H), 3.47 (d, *J* = 31.7 Hz, 4H), 3.20 (d, *J* = 39.6 Hz, 4H), 2.35 (q, *J* = 6.9 Hz, 7H), 1.55 (s, 6H), 1.17 (d, *J* = 6.8 Hz, 12H), 1.08 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.11, 182.33, 153.99, 145.47, 138.89, 134.44, 134.05, 133.92, 130.95, 129.51, 125.49, 124.29, 123.78, 123.66, 66.27, 63.52, 49.35, 43.68, 28.72, 24.28, 24.08, 21.25, 17.11.

Synthesis of 9:





Precursor 4 (40 mg, 0.035 mmol, 1 equiv.) was combined with benzyl amine (12  $\mu$ l, 0.105 mmol, 3 equiv.) and dry TEA (10  $\mu$ l, 0.071 mmol, 2 equiv.) per the general procedure. This gave 9 as a white microcrystalline powder. Crystals were grown using DCM/DEE and via slow diffusion.

**Yield:** 15 mg (40%)

**ESI-HRMS (Acetonitrile) (m/z):** Calculated for  $[C_{49}H_{61}AuN_5O_2]^+$ : 948.4485 observed: 948.4493.

<sup>1</sup>**H NMR (500 MHz, DMSO-***d*<sub>6</sub>) :  $\delta$  8.06 (s, 2H), 7.64 (t, *J* = 6.2 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 2H), 7.50 (d, *J* = 1.9 Hz, 1H), 7.31 (dd, *J* = 7.3, 5.3 Hz, 7H), 7.26 – 7.20 (m, 3H), 6.76 (s, 2H), 4.15 (d, *J* = 6.2 Hz, 2H), 3.80 (d, *J* = 5.2 Hz, 2H), 3.74 (d, *J* = 5.1 Hz, 2H), 2.35 (q, *J* = 6.8, 5.5 Hz, 7H), 1.54 (s, 6H), 1.16 (d, *J* = 6.8 Hz, 12H), 1.08 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.18, 182.32, 155.91, 145.44, 139.99, 138.86, 134.44, 134.14, 133.90, 130.94, 129.48, 128.72, 127.51, 127.32, 125.46, 124.26, 124, 123.56, 63.09, 49.80, 44.24, 28.71, 24.29, 24.07, 21.26, 17.16.

#### Synthesis of 10:



#### Reaction time: 36 h

Precursor 4 (40 mg, 0.035 mmol, 1 equiv.) was combined with pyrene methyl amine hydrochloride (20 mg, 0.075 mmol, 2.1 equiv.) and dry TEA (22  $\mu$ l, 0.170 mmol, 4.8 equiv.) per the general procedure. After the reaction was deemed complete as inferred from an LCMS analysis, the DCM was evaporated off and diethyl ether was added. This produced a white precipitate. The white solid was collected via filtration. The solid isolated in this way was partially dissolved in around 1 ml DCM containing 2 drops of methanol. The mixture was loaded on a silica column and the pure product was collected using 5% methanol in DCM as the eluent;  $R_f \sim 0.4$ . The column can be monitored using an UV lamp with the fluorescent band that elutes second being collected. Conjugate **10** was isolated in the form of a white microcrystalline powder. Crystals were grown from DCM/DEE via slow diffusion.

**Yield:** 17 mg (40%)

**ESI-HRMS (acetonitrile) (m/z):** Calculated for  $[C_{59}H_{65}AuN_5O_2]^+$ : 1072.4798 observed: 1072.4815.

<sup>1</sup>**H** NMR (600 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  8.40 (d, J = 9.2 Hz, 1H), 8.32 – 8.27 (m, 2H), 8.25 (dd, J = 8.6, 3.8 Hz, 2H), 8.14 (s, 2H), 8.07 (t, J = 7.6 Hz, 1H), 7.99 (d, J = 8.1 Hz, 3H), 7.88 (t, J = 6.0 Hz, 1H), 7.52 (d, J = 1.9 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 7.30 (d, J = 1.9 Hz, 1H), 7.21 (d, J = 7.8 Hz, 4H), 6.71 (s, 2H), 4.88 (d, J = 5.9 Hz, 2H), 3.78 (d, J = 5.3 Hz, 2H), 3.73 (d, J = 5.4 Hz, 2H), 2.32 (s, 3H), 2.28 (q, J = 6.9 Hz, 4H), 1.50 (s, 6H), 1.07 (dd, J = 6.9, 5.0 Hz, 12H), 1.01 (d, J = 6.9 Hz, 12H). (Diethyl ether remains with the solid even after overnight vacuum dry, with the crystal too).  $\delta$  3.36 (q), 1.06 (m).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.10, 182.32, 155.80, 145.36, 138.83, 134.35, 134.05, 133.81, 131.24, 130.86, 130.74, 129.43, 128.44, 128.01, 127.81, 127.53, 127.07, 126.72, 125.74, 125.63, 125.39, 125.09, 124.50, 124.38, 124.17, 123.99, 123.60, 63.16, 49.60, 42.60, 28.60, 24.22, 23.97, 21.22, 17.14. (Diethyl ether remains with the solid even after overnight vacuum dry, and with the crystal too). δ 65.63, 15.62.

#### Alternative scheme for aromatic amines (Protocol 2):

**General Protocol 2:** Precursor **4** (1 equiv.) and HOBt (1.5-2 equiv.) were combined in a twonecked round bottom flask and kept under vacuum for 15 min. After that, dry DMF (3 ml) and the amine in question (3-3.5 equiv.) were added. After confirming the completion of the reaction by LCMS, the DMF was concentrated and to the resulting mixture were added DEE and hexanes in excess. The resulting precipitate was then collected by filtration. The solid obtained in this was treated with 6 ml of nanopore water and stirred for another 15 mins at 45 °C. The solid that remained was collected by filtration and washed with first 5 ml of water and then hexanes, respectively.

Synthesis of 11:



#### Reaction time: 48 h

Precursor 4 (35 mg, 0.031 mmol, 1 equiv.) was reacted with <sup>t</sup>Bu Aniline (15  $\mu$ l, 0.093 mmol, 3 equiv.) and HOBt (7 mg, 0.0465 mmol, 1.5 equiv.) per the general Protocol 2. The product was a white powder. Crystals were grown from DCM/DEE via slow diffusion.

**Yield:** 27 mg (77%)

**ESI-HRMS (acetonitrile) (m/z):** Calculated for  $[C_{52}H_{67}AuN_5O_2]^+$ : 990.4955 observed: 990.4972.

<sup>1</sup>**H** NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  9.50 (s, 1H), 8.07 (s, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.56 (d, *J* = 1.8 Hz, 1H), 7.40 – 7.31 (m, 5H), 7.29 (s, 3H), 6.77 (s, 2H), 3.85 (dd, *J* = 21.3, 5.2 Hz, 4H), 2.37 (q, *J* = 5.3, 3.8 Hz, 7H), 1.57 (s, 6H), 1.25 (s, 9H), 1.17 (d, *J* = 6.8 Hz, 12H), 1.10 (d, *J* = 6.9 Hz, 12H).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.16, 182.38, 153.01,145.45, 134.09, 133.91, 130.94, 129.50, 125.82, 125.48, 124.28, 123.67, 118.55, 63.23, 49.90, 34.39, 31.68, 28.73, 24.31, 24.07, 21.26, 17.22.

Synthesis of 12:



#### Reaction time: 48 h

Precursor 4 (40 mg, 0.035 mmol, 1 equiv.) was reacted with N-methylaniline (12  $\mu$ l, 0.11 mmol, 3.1 equiv.) and HOBt (9 mg, 0.07 mmol, 1.5 equiv.) per general Protocol 2. Product **12** was obtained as a white powder. Crystals could be grown from DCM/DEE but they proved too thin to mount for characterization *via* X-ray diffraction analysis.

**Yield:** 14 mg (36%)

**ESI-HRMS (acetonitrile) (m/z):** Calculated for  $[C_{49}H_{61}AuN_5O_2]^+$ : 948.4485 observed: 928.4502.

<sup>1</sup>**H NMR (DMSO-***d*<sub>6</sub>): δ 8.02 (d, J = 1.1 Hz, 2H), 7.54 (t, J = 7.8 Hz, 2H), 7.40 – 7.21 (m, 8H), 7.17 (t, J = 7.0 Hz, 2H), 6.72 (s, 2H), 3.78 (s, 4H), 3.06 (s, 3H), 2.30 (d, J = 8.8 Hz, 7H), 1.48 (s, 6H), 1.12 (d, J = 6.8 Hz, 12H), 1.02 (d, J = 6.8 Hz, 12H).

<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 186.09, 182.24, 154.13, 145.41, 138.84, 134.03, 133.87, 130.90, 129.46, 129.19, 126.43, 125.95, 125.45, 124.26, 123.66, 63.91, 49.58, 37.78, 28.69, 24.22, 24.03, 21.20, 17.11













<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) (25°C): [1][PF<sub>6</sub>]



<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): [1][PF<sub>6</sub>]







<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 4







<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 5



<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) (25°C): 6



<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 6















<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 9



<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>) (25°C): 10



<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 10



<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 11





<sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 12



<sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 12

### **Crystallographic data:**

X-ray experimental for [1][PF<sub>6</sub>] ( $C_{14}H_{18}N_2O$ )Au( $C_{27}H_{36}N_2$ )PF<sub>6</sub>: Crystals grew as large colorless prisms by slow diffusion of diethylether in dichloromethane solution. The data crystal was cut from a larger crystal and had approximate dimensions; 0.30 x 0.21 x 0.086 mm. The data were collected at -173 °C on a Nonius Kappa CCD diffractometer using a Bruker AXS Apex II detector and a graphite monochromator with MoK<sub> $\alpha$ </sub> radiation ( $\lambda = 0.71073$  Å). Reduced temperatures were maintained by use of an Oxford Cryosystems 700 low-temperature device. A total of 2079 frames of data were collected using  $\Box$ -scans with a scan range of 0.6° and a counting time of 23 seconds per frame. Details of crystal data, data collection and structure refinement are listed below. Data reduction were performed using Bruker AXS, Inc's SAINT V827B.<sup>3</sup> The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on F<sup>2</sup> with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.<sup>5</sup> Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in idealized positions.

The structure was refined as a 2-component twin. The twin law was determined using Cell\_Now, data was integrated in SAINT and scaled using TWINABS using the Bruker Apex II software release 2010. The hexafluorophosphate anion was disordered. The disorder was modeled by assigning the variablex to the site occupancy for one component of the disordered anion. The variable (1-x) was assigned to the site occupancy factors of the atoms of the alternate component. A common isotropic displacement parameter was refined for all the fluorine atoms of the two components, with a separate displacement parameter for the phosphorus atoms. The displacement parameters were refined while refining x. Upon convergence of the variable x, the site occupancy factors were fixed and the displacement parameters were allowed to refine. The atoms of the major component were eventually refined anisotropically with their displacement parameters restrained to be approximately isotropic. The atoms of the minor component were refined isotropically. The geometry of the two components was restrained to be equivalent throughout the refinement process.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0324*P)^2]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.0759, with R(F) equal to 0.0398 and a goodness of fit, S, = 1.09. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940593.

Crystal data and structure refinement for [1][PF<sub>6</sub>]

Empirical formula	$\mathrm{C}_{41}\mathrm{H}_{54}\mathrm{Au}\mathrm{F}_{6}\mathrm{N}_{4}\mathrm{O}\mathrm{P}$
Formula weight	960.82
Temperature	100(2) K

Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 11.5799(13) Å	$\alpha = 90.340(7)^{\circ}$ .
	b = 12.395(2) Å	$\beta = 110.629(8)^{\circ}.$
	c = 15.448 Å	$\gamma = 92.601(7)^{\circ}$ .
Volume	2072.4(4) Å <sup>3</sup>	
Z	2	
Density (calculated)	1.540 Mg/m <sup>3</sup>	
Absorption coefficient	3.651 mm <sup>-1</sup>	
F(000)	968	
Crystal size	0.260 x 0.110 x 0.060 mm <sup>3</sup>	
Theta range for data collection	2.191 to 25.423°.	
Index ranges	-13<=h<=13, -14<=k<=14, 0<=l<=18	
Reflections collected	7565	
Independent reflections	7565	
Completeness to theta = $25.242^{\circ}$	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.800	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	7565 / 804 / 528	
Goodness-of-fit on F <sup>2</sup>	1.005	
Final R indices [I>2sigma(I)]	$R_1 = 0.0398, wR_2 = 0.0738$	
R indices (all data)	$R_1 = 0.0494, wR_2 = 0.0759$	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.896 and -1.242 e.Å <sup>-3</sup>	
CCDC no.	1940593	

X-ray experimental for [4]  $(C_{27}H_{36}N_2)Au(C_{21}H_{21}N_3O_5)^{1+}$  PF<sub>6</sub><sup>1-</sup>: Crystals grew as long colorless needles by slow diffusion of diethylether in dichloromethane solution. The data crystal was cut from a larger crystal and had approximate dimensions; 0.36 x 0.12 x 0.094 mm. The data were collected at -173 °C on a Nonius Kappa CCD diffractometer using a Bruker AXS Apex II detector and a graphite monochromator with MoK<sub> $\alpha$ </sub> radiation ( $\lambda = 0.71073$  Å). Reduced temperatures were maintained by use of an Oxford Cryosystems 700 low-temperature device. A total of 2886 frames of data were collected using  $\omega$ -scans with a scan range of 0.6° and a counting time of 18 seconds per frame. Details of crystal data, data collection and structure refinement are listed below. Data reduction was performed using Bruker AXS, Inc's SAINT V827B.<sup>3</sup> The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on F<sup>2</sup> with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.<sup>5</sup> Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in idealized positions.

The methyl groups on an isopropyl group were disordered. The disorder was modeled by assigning the variable x to the site occupancy factors for the carbon atoms of one component of the disorder. The variable, 1-x, was assigned to the site occupancy factors for the alternate carbon atoms. A common isotropic displacement factor was refined for the four carbon atoms while refining x. Upon convergence of x, the site occupancy factors were fixed and the displacement parameters for the carbon atoms were refined. The geometry of the affected methyl groups was restrained to be equivalent throughout the refinement process.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0276*P)^2 + (10.5766*P)]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.0821, with R(F) equal to 0.0330 and a goodness of fit, S, = 1.08. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940596.

Crystal data	and structure	refinement for 4	ł

Empirical formula	C <sub>48</sub> H <sub>57</sub> Au F <sub>6</sub> N <sub>5</sub> O <sub>5</sub> P	
Formula weight	1125.92	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 10.6871(4) Å	$\alpha = 110.760(3)^{\circ}$ .
	b = 15.3640(6) Å	$\beta = 92.833(3)^{\circ}$ .
	c = 16.2640(5)  Å	$\gamma = 99.200(3)^{\circ}$ .
Volume	2448.65(16) Å <sup>3</sup>	
Ζ	2	
Density (calculated)	1.527 Mg/m <sup>3</sup>	
Absorption coefficient	3.109 mm <sup>-1</sup>	
F(000)	1136	
Crystal size	0.361 x 0.125 x 0.094 mr	n <sup>3</sup>
Theta range for data collection	2.190 to 25.120°.	

Index ranges	-12<=h<=12, -18<=k<=18, -19<=l<=19
Reflections collected	72168
Independent reflections	8735 [R(int) = 0.0558]
Completeness to theta = $25.120^{\circ}$	99.9 %
Absorption correction	Numerical
Max. and min. transmission	0.7966 and 0.4068
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	8735 / 419 / 626
Goodness-of-fit on F <sup>2</sup>	1.081
Final R indices [I>2sigma(I)]	$R_1 = 0.0330, wR_2 = 0.0802$
R indices (all data)	$R_1 = 0.0359, wR_2 = 0.0821$
Extinction coefficient	n/a
Largest diff. peak and hole	2.863 and -2.302 e.Å <sup>-3</sup>
CCDC number	1940596

X-ray experimental for complex [5]  $(C_{15}H_{17}N_4O_2)Au(C_{27}H_{36}N_2)^{1+\bullet}PF_6^{1-}$ : Crystals grew as colorless needles by slow diffusion of diethylether in dichloromethane solution. The data crystal was cut from a larger crystal and had approximate dimensions; 0.17 x 0.09 x 0.04 mm. The data were collected on an Agilent Technologies SuperNova Dual Source diffractometer using a µ-focus Cu K<sub> $\alpha$ </sub> radiation source ( $\lambda = 1.5418$  Å) with collimating mirror monochromators. A total of 1269 frames of data were collected using  $\omega$ -scans with a scan range of 1° and a counting time of 3 seconds per frame with a detector offset of +/- 41.7° and 8 seconds per frame with a detector offset of +/- 111.0°. The data were collected at 100 K using an Oxford 700 Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed below. Data collection, unit cell refinement and data reduction were performed using Agilent Technologies CrysAlisPro V 1.171.39.46.11 The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on  $F^2$  with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.5 Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The hydrogen atoms bound to the nitrogen atoms, N5 and N11, were located in a  $\Delta F$  map and refined with isotropic displacement parameters. The hydrogen atoms on the terminal nitrogen atoms, N6 and N12, were difficult to locate in the difference electron density map. Three hydrogen atoms were added to both N6 and N12 in an idealized, tetrahedral arrangement using an AFIX 137 instruction. After a few cycles of refinement, the constraint on the displacement parameters was removed and the isotropic displacement parameters for these six H atoms was allowed to refine. Because there were only two H atoms attached to each of the nitrogen atoms, one H atom on each nitrogen was expected to have unreasonably high displacement parameters, which in fact was what was observed. This H atom was removed from the refinement model.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0614*P)^2 + (3.6544*P)]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.109, with R(F) equal to 0.0399 and a goodness of fit, S, = 1.04. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940595.

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Empirical formula	$C_{42}H_{56}AuF_6N_6O_2P$		
Formula weight	1018.86	1018.86	
Temperature	100(2) K	100(2) K	
Wavelength	1.54184 Å	1.54184 Å	
Crystal system	triclinic		
Space group	P -1		
Unit cell dimensions	a = 11.0823(2) Å	α= 70.377(2)°.	
	b = 17.7057(4) Å	β= 88.2690(10)°.	
	c = 24.2599(4)  Å	$\gamma = 79.328(2)^{\circ}$ .	
Volume	4403.63(16) Å <sup>3</sup>		
Z	4		
Density (calculated)	1.537 Mg/m <sup>3</sup>		
Absorption coefficient	7.196 mm <sup>-1</sup>	7.196 mm <sup>-1</sup>	
F(000)	2056		
Crystal size	0.230 x 0.090 x 0.050 m	m <sup>3</sup>	
Theta range for data collection	2.697 to 75.985°.		
Index ranges	-13<=h<=13, -22<=k<=	-13<=h<=13, -22<=k<=21, -30<=l<=21	
Reflections collected	53753	53753	
Independent reflections	18005 [R(int) = 0.0538]	18005 [R(int) = 0.0538]	
Completeness to theta = $67.684^{\circ}$	100.0 %	100.0 %	
Absorption correction	Gaussian and multi-scan	Gaussian and multi-scan	
Max. and min. transmission	1.00 and 0.503	1.00 and 0.503	
Refinement method	Full-matrix least-squares	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	18005 / 13 / 1087		
Goodness-of-fit on F <sup>2</sup>	1.036		

Crystal data and structure refinement for 5

Final R indices [I>2sigma(I)]	$R_1 = 0.0399, wR_2 = 0.1019$
R indices (all data)	$R_1 = 0.0468, wR_2 = 0.1090$
Extinction coefficient	n/a
Largest diff. peak and hole	1.289 and -1.338 e.Å-3
CCDC number	1940595

X-ray experimental for complex [8]  $(C_{19}H_{25}N_3O_3)Au(C_{27}H_{36}N_2)^{1+\bullet}PF_6^{1-}$ : Crystals grew as colorless needles by slow diffusion of diethylether in dichloromethane solution. The data crystal was cut from a larger crystal and had approximate dimensions; 0.18 x 0.064 x 0.046 mm. The data were collected on an Agilent Technologies SuperNova Dual Source diffractometer using a µ-focus Cu K<sub> $\alpha$ </sub> radiation source ( $\lambda = 1.5418$  Å) with collimating mirror monochromators. A total of 5147 frames of data were collected using  $\omega$ -scans with a scan range of 1° and a counting time of 3 seconds per frame with a detector offset of +/- 42.7° and 11 seconds per frame with a detector offset of +/- 111.0°. The data were collected at 100 K using an Oxford 700 Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed below. Data collection, unit cell refinement and data reduction were performed using Agilent Technologies CrysAlisPro V 1.171.39.46.<sup>11</sup> The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on F<sup>2</sup> with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.5 Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms).

There are two Au complexes in the asymmetric unit. In one, the morpholine carboxylate group is disordered. Also, one of the hexafluorophosphate anions is disordered as well. The disorder was modeled in a similar manner for both species. For example for the hexafluorophosphate ion, the variable x was assigned to the site occupancy factors for one component of the disordered ion. For the second component, the variable (1-x) was assigned to the site occupancy factors. A common isotropic displacement parameter was refined for the fluorine atoms of both components while refining the variable x. At the same time, the displacement parameters for the phosphorus atoms were constrained to be equal but not necessarily the same as that for the fluorine atoms. The geometry of the two ions was restrained to be equivalent throughout the refinement procedure. Upon convergence of the variable x, the site occupancy factors were fixed at the appropriate value and the atoms were refined while being restrained to be approximately equal.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0819*P)^2 + (5.351*P)]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.120, with R(F) equal to 0.0431 and a goodness of fit, S, = 1.02. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940598.

Crystal data	and	structure	refinement	for	8
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Empirical formula	C <sub>46</sub> H <sub>61</sub> Au F <sub>6</sub> N <sub>5</sub> O <sub>3</sub> P	
Formula weight	1073.93	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 11.0059(5) Å	$\alpha = 100.792(3)^{\circ}$ .
	b = 18.0147(9) Å	$\beta = 96.933(3)^{\circ}$ .
	c = 25.0303(7) Å	$\gamma = 99.946(4)^{\circ}$ .
Volume	4741.2(4) Å <sup>3</sup>	
Ζ	4	
Density (calculated)	1.505 Mg/m <sup>3</sup>	
Absorption coefficient	6.726 mm <sup>-1</sup>	
F(000)	2176	
Crystal size	0.180 x 0.064 x 0.046 mm <sup>3</sup>	
Theta range for data collection	2.549 to 68.328°.	
Index ranges	-13<=h<=13, -21<=k<=21, -30<=l<=28	
Reflections collected	147445	
Independent reflections	17383 [R(int) = 0.1074]	
Completeness to theta = $67.684^{\circ}$	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.555	
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	17383 / 1337 / 1291	
Goodness-of-fit on F <sup>2</sup>	1.019	
Final R indices [I>2sigma(I)]	$R_1 = 0.0431, wR_2 = 0.1143$	
R indices (all data)	$R_1 = 0.0473, wR_2 = 0.1198$	
Extinction coefficient	n/a	
Largest diff. peak and hole	2.361 and -1.533 e.Å <sup>-3</sup>	
CCDC number	1940598	

X-ray experimental for complex [9]  $(C_{27}H_{36}N_2)Au(C_{22}H_{25}N_3O_2) - \frac{1}{4} CH_2Cl_2$ : Crystals grew as thin, colorless needles by vapor diffusion of diethyl ether into a dichloromethane solution. The data crystal was cut from a much longer crystal and had approximate dimensions; 0.20 x 0.049 x 0.037 mm. The data were collected on an Agilent Technologies SuperNova Dual Source

diffractometer using a  $\mu$ -focus Cu K<sub> $\alpha$ </sub> radiation source ( $\lambda = 1.5418$  Å) with collimating mirror monochromators. A total of 1028 frames of data were collected using  $\omega$ -scans with a scan range of 1° and a counting time of 14 seconds per frame with a detector offset of +/- 41.6° and 40 seconds per frame with a detector offset of 112.0°. The data were collected at 100 K using an Oxford 700 Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed below. Data collection, unit cell refinement and data reduction were performed using Rigaku Oxford Diffraction's CrysAlisPro V 1.171.40.37a.<sup>11</sup> The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on F<sup>2</sup> with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.<sup>5</sup> Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms).

There are two Au complexes in the asymmetric unit. Both have some portion of the complex that is disordered. In one Au complex, the benzyl carbamate portion of the carbene is disordered. In the other Au complex, the entire carbene complex including the carbamate and the mesitylene groups and the Au ion is disordered. Due to the proximity of the disordered groups to a crystallographic inversion center, the site occupancy factors were set to  $\frac{1}{2}$ . It appeared near the benzyl group, that a small amount of DCM was present.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0582*P)^2 + (0.4412*P)]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.145, with R(F) equal to 0.0540 and a goodness of fit, S, = 1.02. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940594.

Empirical formula	C49 H61 Au Cl0.50 F6 N5 O2 P		
Formula weight	1111.69		
Temperature	100(2) K		
Wavelength	1.54184 Å		
Crystal system	triclinic		
Space group	P -1		
Unit cell dimensions	a = 11.1145(6) Å	$\alpha = 83.682(4)^{\circ}.$	
	b = 18.0534(9) Å	$\beta = 84.131(5)^{\circ}.$	
	c = 25.6124(14)  Å	$\gamma = 78.693(5)^{\circ}$ .	
Volume	4991.7(5) Å <sup>3</sup>		
Z	4		
Density (calculated)	1.479 Mg/m <sup>3</sup>		
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Absorption coefficient	6.636 mm <sup>-1</sup>
F(000)	2250
Crystal size	$0.197 \ge 0.049 \ge 0.037 \text{ mm}^3$
Theta range for data collection	2.918 to 69.032°.
Index ranges	-13<=h<=12, -21<=k<=21, -30<=l<=20
Reflections collected	28263
Independent reflections	18007 [R(int) = 0.0522]
Completeness to theta = $67.684^{\circ}$	98.4 %
Absorption correction	Gaussian and multi-scan
Max. and min. transmission	1.00 and 0.563
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	18007 / 1851 / 1565
Goodness-of-fit on F <sup>2</sup>	1.024
Final R indices [I>2sigma(I)]	$R_1 = 0.0540, wR_2 = 0.1264$
R indices (all data)	$R_1 = 0.0821, wR_2 = 0.1447$
Extinction coefficient	n/a
Largest diff. peak and hole	1.102 and -1.270 e.Å <sup>-3</sup>
CCDC no.	1940594.

X-ray Experimental for [10] (C<sub>32</sub>H<sub>29</sub>N<sub>3</sub>O<sub>2</sub>)Au(C<sub>27</sub>H<sub>36</sub>N<sub>2</sub>)•PF<sub>6</sub>: Crystals grew as colorless prisms by vapor diffusion of diethyl ether into a dichloromethane solution. The data crystal had approximate dimensions; 0.2 x 0.1 x 0.04 mm. The data were collected on a Rigaku AFC12 diffractometer with a Saturn 724+ CCD using a graphite monochromator with MoK<sub> $\alpha$ </sub> radiation ( $\lambda$ = 0.71073 Å). A total of 1644 frames of data were collected using  $\omega$ -scans with a scan range of 0.5° and a counting time of 30 seconds per frame. The data were collected at 100 K using an Rigaku XStream Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in below. Data collection were performed using the Rigaku Americas Corporation's Crystal Clear version 1.40.12 Unit cell refinement and data reduction were performed using Rigaku Oxford Diffraction's CrysAlisPro V 1.171.39.46.11 The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on F<sup>2</sup> with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.5 Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The hydrogen atom bound to N5 was located in a  $\Delta F$  map and refined with an isotropic displacement parameter.

A molecule of what appeared to be diethyl ether was disordered. The disordered could not be satisfactorily modeled. The program, SQUEEZE,<sup>13</sup> as incorporated into PLATON, was used to remove the contributions to the scattering factors due to the disordered solvent.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0234*P)^2 + (0.8711*P)]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.0478, with R(F) equal to 0.0227 and a goodness of fit, S, = 1.02. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940599.

Empirical formula	$C_{59} H_{65} Au F_6 N_5 O_2 P$			
Formula weight	1218.09			
Temperature	100(2) K			
Wavelength	0.71073 Å			
Crystal system	monoclinic			
Space group	P 21			
Unit cell dimensions	a = 11.0376(11) Å	<i>α</i> = 90°.		
	b = 22.224(2) Å	β= 94.2560(10)°.		
	c = 12.1752(14) Å	$\gamma = 90^{\circ}$ .		
Volume	2978.3(5) Å <sup>3</sup>			
Z	2			
Density (calculated)	1.358 Mg/m <sup>3</sup>			
Absorption coefficient	2.559 mm <sup>-1</sup>			
F(000)	1236			
Crystal size	0.2 x 0.1 x 0.04 mm <sup>3</sup>			
Theta range for data collection	1.677 to 27.484°.			
Index ranges	-14<=h<=14, -28<=k<=28, -15<=l<=15			
Reflections collected	57083			
Independent reflections	13589 [R(int) = $0.0363$ ]			
Completeness to theta = $25.242^{\circ}$	100.0 %			
Absorption correction	Semi-empirical from equivalents			
Max. and min. transmission	1.00 and 0.720			
Refinement method	Full-matrix least-squares on F <sup>2</sup>			
Data / restraints / parameters	13589 / 2 / 683			
Goodness-of-fit on F <sup>2</sup>	1.024			
Final R indices [I>2sigma(I)]	$R_1 = 0.0227, wR_2 = 0.0470$			

R indices (all data)	$R_1 = 0.0255, wR_2 = 0.0478$
Absolute structure parameter	0.187(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.559 and -0.462 e.Å $^{-3}$
CCDC no.	1940599

X-ray experimental for [11]  $(C_{25}H_{31}N_{3}O_{2})Au(C_{16}H_{36}N_{2})^{1+}\bullet PF_{6}^{1-}\bullet \frac{1}{2}H_{2}O$ : Crystals grew as colorless laths by vapor diffusion of di-isopropyl ether into dichloromethane. The data crystal was cut from a larger crystal and had approximate dimensions; 0.14 x 0.051 x 0.026 mm. The data were collected on an Agilent Technologies SuperNova Dual Source diffractometer using a µ-focus  $CuK_{\alpha}$  radiation source ( $\lambda = 1.5418$  Å) with collimating mirror monochromators. A total of 475 frames of data were collected using  $\omega$ -scans with a scan range of 1° and a counting time of 18 seconds per frame using a detector offset of 0.0°, a counting time of 47.5 seconds per frame using a detector offset of +/- 56.4° and 95 seconds with a detector offset of 112.7°. The data were collected at 100 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed below. Data collection, unit cell refinement and data reduction were performed using Rigaku Oxford Diffraction's CrysAlisPro V 1.171.40-64.37a.11 The structure was solved by direct methods using SHELXT<sup>4</sup> and refined by full-matrix least-squares on  $F^2$  with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.5 Structure analysis was aided by use of the programs PLATON<sup>6</sup> and WinGX.<sup>7</sup> The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms).

A molecule of di-isopropyl ether and a region of highly diffuse solvent were excluded from the refinement when a satisfactory model to these disordered groups could not be obtained. The contributions to the scattering factors due to this solvent molecule were removed by use of the utility SQUEEZE<sup>13</sup> in PLATON. PLATON was used as incorporated in WinGX.

The function,  $\Sigma w(|F_0|^2 - |F_c|^2)^2$ , was minimized, where  $w = 1/[(\sigma(F_0))^2 + (0.0778*P)^2]$  and  $P = (|F_0|^2 + 2|F_c|^2)/3$ .  $R_w(F^2)$  refined to 0.240, with R(F) equal to 0.0887 and a goodness of fit, S, = 1.02. Definitions used for calculating R(F),  $R_w(F^2)$  and the goodness of fit, S, are given below.<sup>8</sup> The data were checked for secondary extinction effects but no correction was necessary. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).<sup>9</sup> All figures were generated using SHELXTL/PC.<sup>10</sup> Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found in the cif file. This file may be downloaded from the Cambridge Crytallographic Data Centre by making reference to CCDC number 1940597.

Crystal data and structure refinement for 11

Empirical formula	$C_{52}H_{68}AuF_6N_5O_{2.5}P$
Formula weight	1145.05
Temperature	100(2) K
Wavelength	1.54184 Å
<b>S46  </b> P a g e	

Crystal system	orthorhombic		
Space group	P b c a		
Unit cell dimensions	$a = 43.9057(11) \text{ Å}$ $\alpha = 9$	90°.	
	$b = 11.3191(4) \text{ Å}$ $\beta = 9$	€0°.	
	$c = 47.4794(9) \text{ Å}$ $\gamma = 9$	0°.	
Volume	23596.0(11) Å <sup>3</sup>		
Z	16		
Density (calculated)	1.289 Mg/m <sup>3</sup>		
Absorption coefficient	5.432 mm <sup>-1</sup>		
F(000)	9328		
Crystal size	0.140 x 0.051 x 0.026 mm <sup>3</sup>		
Theta range for data collection	3.548 to 74.046°.		
Index ranges	-27<=h<=54, -13<=k<=13, -59<=l<=58		
Reflections collected	50108		
Independent reflections	23089 [R(int) = 0.0945]		
Completeness to theta = $67.684^{\circ}$	99.1%		
Absorption correction	Numerical and multi-scan		
Max. and min. transmission	1.00 and 0.342		
Refinement method	Full-matrix least-squares on F <sup>2</sup>		
Data / restraints / parameters	23089 / 1902 / 1247		
Goodness-of-fit on F <sup>2</sup>	1.020		
Final R indices [I>2sigma(I)]	$R_1 = 0.0887, wR_2 = 0.1976$		
R indices (all data)	$R_1 = 0.1471, wR_2 = 0.2398$		
Extinction coefficient	n/a		
Largest diff. peak and hole	2.703 and -1.995 e.Å <sup>-3</sup>		
CCDC number	1940597		

# **ORTEP** representations of crystals obtained:



A: ORTEP representation of  $[1][PF_6]$  rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



B: ORTEP representation of 4, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



C: ORTEP representation of 5, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



D: ORTEP representation of 8, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



E: ORTEP representation of 9, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



F: ORTEP representation of 10, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.



G: ORTEP representation of 11, rendered using POV-Ray. Thermal ellipsoid plots are drawn at 50% probability level.

## **Biological study details:**

**Cell proliferation studies**: A549 Cells were harvested and seeded into 96-well culture plates (Costar 07-200-90) in 100  $\mu$ L of culture media. They were allowed to incubate overnight at 37 °C in the presence of 5% CO<sub>2</sub>. A549 cells were seeded at a density of 1500 cells/well. The next day, appropriate serial dilutions of drug stocks in culture media were made. To each well of a 96 well plate was added 100  $\mu$ L of the appropriate solution. After a total of three days, a 50 mL aliquot of 3 mg/mL tetrazolium dye, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (Alfa Aesar L11939) was added to each well, followed by a 4 h incubation period at 37 °C. After removal of the medium, the resulting formazan was dissolved in 50 mL DMSO and the respective absorbances were measured at 560 – 650 nm using a microplate reader (Molecular Devices, Sunnyvale, CA). Absorbance values were corrected for background and then normalized to wells containing untreated cells to allow for plate-to-plate comparisons. Resulting dose response curves were subjected to linear regression analysis (Origin by OriginLab, Inc.) for determination of IC<sub>50</sub> values. The data are shown as mean inhibition of proliferation or growth as a percentage of control cells and are from 2 – 3 replicate experiments.

Compounds	IC <sub>50</sub> (μM)	Standard deviation (±)
Auranofin	2.18114	0.14796
1•PF <sub>6</sub>	0.14813	0.01836
5	0.39418	0.02907
7	0.56166	0.02204
Doxorubicin•HCl	0.1311	0.03655
8	0.10905	0.01428
10	0.213	0.01206
11	0.15341	0.01086

**Table S1:** Combined listing of  $IC_{50}$  values of different conjugates after 72 h treatment of A549 lung cancer cell line (maximum concentration of DMSO: 0.1%). This concentration of DMSO was determined to be non-toxic in separate control experiments.



**Fig. S4.** Cell proliferation profiles of A549 lung cancer cells treated with 7 and doxorubicin (72 h drug incubation time). Auranofin has been used as a reference drug. (Maximum DMSO: 0.1%.)

#### **Lipoate Reduction Assay:**

*Reagent Preparation:* 20 mg of lipoic acid was dissolved in 600  $\mu$ L of PEG 400 and 400  $\mu$ L of DPBS to make a 97 mM stock solution. In a separate vial, 7.1 mg of sodium phosphate anhydrous (dibasic) was added to 9.49 mL HBSS (Life tech 14025-092), resulting in 5 mM solution. From the lipoic acid stock solution, 0.51 mL was slowly transferred into HBSS containing phosphate buffer solution. The final concentration of lipoic acid was 5 mM. To this mixture was added 3.96 mg of DTNB which gave 1 mM solution. Finally, the mixture was sonicated several times and heated at 40° C for 5 mins to ensure complete dissolution of DTNB. The solution was passed through a sterile 0.2 micron filter.

*Live Cell Imaging Assay:* A549 cells were harvested and seeded at a density of 10,000 cells/well in 96-well culture plates. Following an overnight incubation at 37°C and 5% CO2, appropriate serial dilutions of drug stocks in culture media were performed, and 100  $\mu$ L of the appropriate solution were added to each well. Cells were further incubated for 6 h. Thereafter, the media solution was removed from each well and washed with 200  $\mu$ L of HBSS solution. Finally, 100  $\mu$ L of 5 mM Lipoate (Tokyo Chemical Industry Co., Ltd. L0207) and 1 mM of DTNB (Acros Organics 117540050) solution were added to each well. The absorbance of each well at 405 nm was recorded immediately and once every 20 min for three hours on a microplate reader. Plates were covered with aluminum foil between readings.



Fig. S5. Lipoate reduction assay as a method to assess thioredoxin reductase activity. This time dependent live cell imaging assay was conducted with 1.25  $\mu$ M of respective complex in A549 lung cancer cells.

Students unpaired T-test of data at 180 min								
	Auranofin	conj 5	conj 8	conj 11	1*PF6	conj 10	conj 7	Dox
Control vs	1.38E-12	2.43E-12	4.76E-14	7.85E-06	3.10E-14	1.81E-10	0.03	9.20E-04
Auanofin vs	1.00	0.94	2.10E-08	0.60	0.01	2.94E-03	1.17E-10	3.66E-19
Dox vs	3.66E-19	4.49E-17	1.21E-20	1.60E-18	1.90E-20	4.64E-18	6.53E-07	1.00

**Table S2.** Statistical assessment of thioredoxin reductase inhibition from each respective complex after 180 min of monitoring (comparisons that were not statistically significant have been shown in italics).

**Fluorescence microscopy:** Tumor cells were harvested and seeded at a density of  $2x10^5$  cells/dish in 35 mm dishes containing a poly-D lysine coated 10 mm glass diameter (Mat Tek P35GC-1.5-10-C) overnight. Cells were then incubated with respective doses of different complexes at 37 °C 4-7 h. Post incubation, the media was removed and cells were washed (2x) with PBS. To the cells was added a PBS solution containing 1µg/mL Hoechst 33342 (Lifetech H1399) and 50 nM Mitotracker Red FM (Lifetech M22425) for 30 min at 37 °C. After incubation, the dye PBS solution was removed and cells were washed with PBS (2x). Cells were then imaged fluorescently on a Leica SP5 X White light laser confocal microscope. Images were taken with a 63X, NA 1.4 objective.

## Additional experimental data:



Fig. S6. Excitation and emission spectra of 10 (33 µM in 1% DMSO/water)



Fig. S7. Excitation and emission spectra of  $10 (5 \mu M \text{ in DMSO})$ 



Fig. S8. Fluorescence produced by 10 when excited at 354 nm (33  $\mu$ M in 1% DMSO/water solution)



Fluorescence data for Au(I)-NHC-DOX conjugate 7:



**Fig. S9.** Excitation and emission spectra of 7 (10  $\mu$ M in DMSO)

Fig. S10. Excitation and emission spectra of 7 (20  $\mu$ M in 1% DMSO/H<sub>2</sub>O)



**Fig. S11.** Fluorescence intensity comparison: (yellow) 1% PBS DMSO mixture emission [slit width 10 mm], excited at 405 nm. (blue) Emission of 10 in 1% PBS DMSO mixture [slit width 10], excited at 405 nm. Orange: Emission of 7 in 1% PBS DMSO mixture [slit width 5 mm], excited at 502 nm. This study compares the fluorescent output of 7 and 10 under confocal microscopy conditions where excitation of each fluorophore is limited to 405 nm or greater. Because of this, the fluorescent output of 10, possessing a  $\lambda_{max}$  of 342 nm, was significantly reduced when excited at 405 nm. However, 7 was excited at the  $\lambda_{max}$  of 502 nm and a resulting strong fluorescent output is observed and was also observed in the confocal microscopy images detailed below.



**Fig. S12.** Confocal microscopy images of A549 human lung cancer cell line treated with **10** for 7 h. (a) Mitotracker Red channel (excited at 588 nm) (b) **10** (excited at 405 nm) (c) Merged image. The overlap indicates that **10** localizes to the mitochondria.



**Fig. S13.** Confocal microscopy images of A549 human lung cancer cell line treated with only 7 at 5  $\mu$ M for 6 h. (a) Mitotracker Red channel (excited at 588 nm) (b) 8 (excited at 502 nm) (c) Merged image. This study indicates that there is no fluorescent interference between 7 and the Mitotracker Red channel.



Fig. S14. Confocal microscopy images of A549 human lung cancer cell line treated with only 7 for 6 h imaged at two different concentrations: (a) 1  $\mu$ M (b) 500 nM.



**Fig. S15.** Confocal microscopy images of A549 human lung cancer cells treated with 5  $\mu$ M of Au(I)-NHC-Dox conjugate 7, 5  $\mu$ M doxorubicin and vehicle only for 6 h. The nuclear overlay of doxorubicin and the Hoechst dye suggests the nuclear localization of doxorubicin. However, no overlay was observed between 7 and the Hoechst dye leading us to suggest that 7 does not localize to the nucleus.

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- 8)  $\begin{aligned} R_{W}(F^{2}) &= \{ \Sigma w(|F_{0}|^{2} |F_{c}|^{2})^{2} / \Sigma w(|F_{0}|)^{4} \}^{1/2} \text{ where w is the weight given each} \\ \text{reflection.} \\ R(F) &= \Sigma (|F_{0}| |F_{c}|) / \Sigma |F_{0}| \} \text{ for reflections with } F_{0} > 4(\sigma(F_{0})). \\ S &= [\Sigma w(|F_{0}|^{2} |F_{c}|^{2})^{2} / (n p)]^{1/2}, \text{ where n is the number of reflections and p is the number of reflections and p is the number of reflections.} \end{aligned}$
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